CLAIMS

A compound of formula I or the quaternized form thereof

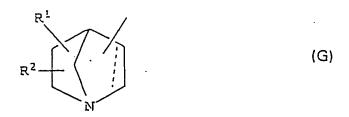
 $G-(CH_2)_{\Xi}-W$ N N (I)

wherein W is oxygen or sulphur; R is selected from the group consisting of hydrogen, amino, halogen, NHR⁶, NR⁶R⁷, R⁴, -OR⁴, -SR⁴, -SOR⁴, -SO₂R⁴, C₃₋₁₀cycloalkyl, C₄₋₁₂-(cycloalkylalkyl), -Z-C₃₋₁₀-cycloalkyl and -Z-C₄₋₁₂-(cycloalkylalkyl) which is optionally substituted with C₁₋₆-alkyl; R⁴ is selected from the group consisting of C_{1-15} -alkyl, C_{2-15} -alkenyl, C_{2-15} -alkynyl and C_{4-15} -alkenynyl, each of which is optionally substituted with one or more independently selected from the group consisting of halogen(s), -CF₃, -CN, Y, phenyl and phenoxy wherein phenyl or phenoxy is optionally substituted with one or more independently selected from the group consisting of -OH, halogen, -NO₂, -CN, C₁₋₄-alkyl, C₁₋₄-alkylthio, C₁₋₄alkoxy, -SCF₃, -OCF₃, -CF₃, -CONH₂ and -CSNH₂; or R is phenyl or benzyloxycarbonyl, each of which is optionally substituted with one or more independently selected from the group consisting of halogen, -CN, C1-4-alkyl, C1-4-alkoxy, -OCF3, -CF3, -CONH2 and -CSNH2; or R is selected from the group consisting of -OR5Y, -SR⁵Y, OR⁵ZY, -SR⁵ZY, -OR⁵ZR⁴ and -SR⁵ZR⁴; Z is oxygen or sulphur; R⁵ is C₁₋₁₅alkylene, C2-15-alkenylene, C2-15-alkynylene or C4-15-alkenynylene; Y is a 5 or 6 membered heterocyclic group optionally substituted with one or more independently selected from the group consisting of -OH, halogen, -NO2, -CN, C1-4-alkyl,

C₁₋₄-alkylthio, C₁₋₄-alkoxy, -SCF₃, -OCF₃, -CF₃, -CONH₂ and -CSNH₂; G is

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 R^6 and R^7 independently are selected from the group consisting of hydrogen and $C_{1.6}$ -alkyl; or R^6 and R^7 together with the nitrogen atom optionally form a 4- to 6-membered ring; R^1 and R^2 independently are selected from the group consisting of hydrogen, -OH, = O, C_{1-15} -alkyl, C_{2-15} -alkenyl, C_{2-15} -alkynyl, C_{1-10} -alkoxy, and C_{1-10} -alkyl substituted with one or more independently selected from the group consisting of -OH, -COR⁸, -CH₂OH, halogen, -NH₂, carboxy and phenyl; R^8 is hydrogen, C_{1-6} -alkyl; r is 0, 1 or 2; is a single or double bond; or a pharmaceutically acceptable salt or solvate thereof.

- 2. A compound of claim 1 wherein G is saturated.
- 3. A compound according to claim 1 or 2 wherein G is

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and wherein the -(CH₂),-W-thiadiazole is attached to the 3- or 4-position of G.

4. A compound according to anyone of the preceeding claims wherein G is

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- 5. A compound according to anyone of the preceeding claims wherein r is 0.
- 6. A compound according to anyone of the preceeding claims wherein W is oxygen.

7. A compound according to anyone of the preceding claims wherein R is $-OR^4$, $-SR^4$, $-SO_2R^4$, $-Z-C_{3-10}$ -cycloalkyl or $-Z-C_{4-12}$ -(cycloalkylalkyl) which is optionally substituted with C_{1-6} -alkyl or R is $-OR^5Y$, $-SR^5Y$, $-OR^5ZY$, $-SR^5ZY$, $-OR^5ZR^4$ or $-SR^5ZR^4$, wherein R^4 , R^5 , Z and Y are as defined above.

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8. A compound according to anyone of the preceding claims wherein R is $-OR^4$, $-SR^4$, $-OR^5ZY$, $-SR^5ZY$, $-OR^5ZR^4$ or $-SR^5ZR^4$, wherein R⁴, R⁵, Z and Y are as defined above.

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9. A compound according to anyone of the preceding claims wherein R^4 is C_{1-15} -alkyl, C_{2-15} -alkenyl, C_{2-15} -alkynyl or C_{4-15} -alkenynyl, each of which is optionally substituted with one or more independently selected from the group consisting of halogen(s), -CF₃, -CN, Y and phenyl which is optionally substituted with one or or more independently selected from the group consisting of -OH, halogen, -CN, C_{1-4} -alkyl, C_{1-4} -alkylthio, C_{1-4} -alkoxy, -SCF₃, -OCF₃, and CF₃, wherein Y is as defined above.

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10. A compound according to anyone of the preceding claims wherein R is - OR^4 or -SR⁴, wherein R⁴ is straight or branched C_{2-8} -alkynyl substituted with phenyl or Y each of which is optionally substituted with -OH, halogen, -NO₂, -CN, C_{1-4} -alkyl, C_{1-4} -alkylthio, C_{1-4} -alkoxy, -SCF₃, -OCF₃, -CF₃, -CONH₂ or -CSNH₂, wherein Y is as defined above.

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- 11. A compound according to anyone of the preceding claims wherein R is $-OR^4$ or $-SR^4$, wherein R^4 is propynyl substituted with phenyl, thiophene, pyridine, furan or thiazole each of which is optionally substituted with halogen, -CN, C_{1-4} -alkoxy or $-OCF_3$.
- 12. A compound according to claim 1 which is selected from the following:

Endo 3-(3-butylthio-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-propylthio-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-propylsulfonyl-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-(4-fluorophenyl)-2-propynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-phenyl-2-propynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabi-cyclo[2.2.1]heptane,

Endo 3-(3-[3-(3-methoxyphenyl)-2-propynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-methyl-2-butenyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicy-clo[2.2.1]heptane,

Endo 3-(3-[2-cyclopropylethyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabi-cyclo[2.2.1]heptane,

Endo 3-(3-[4-fluorobenzyloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[2-butynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

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Endo 3-(3-methylthioethoxy-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,

Endo 3-(3-methoxyethoxy-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

19940953 MORROL Endo 3-(3-[4-trifluoromethoxybenzyloxy]-1,2,5-thiadiazol-4-yloxy)-1-

azabicyclo[2.2.1]heptane,

Endo 3-(3-[4,4,4-trifluorobutyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabi-

cyclo[2.2.1]heptane,

Endo 3-(3-[2-fluoro-4-(trifluoromethyl)-benzyloxy]-1,2,5-thiadiazol-4-yloxy)-1-

azabicyclo[2.2.1]heptane,

Endo 3-(3-[4-(3-methoxyphenyl)-3-butyn-2-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-20

azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-(4-chlorophenyl)-2-propynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-

azabicyclo[2.2.1]heptane,

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Endo 3-(3-[1-(3-methoxyphenyl)-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-

azabicyclo[2.2.1]heptane,

Endo 3-(3-[1-(3-methoxyphenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-

yloxy)-1-azabicyclo[2.2.1]heptane,

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Endo 3-(3-[2,2,2-trifluoroethyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabi-cyclo[2.2.1]heptane,

Endo 3-(3-cyclobutylmethyloxy-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-5 [2.2.1]heptane,

Endo 3-(3-(3-(3-trifluoromethylphenyl)-2-propynyl-1-oxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo (Z)-3-(3-(5-(4-fluorophenyl)-3-methyl-2-penten-4-yn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo (E)-3-(3-(5-(4-fluorophenyl)-3-methyl-2-penten-4-yn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-(3-pyridyl)-2-propyn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo (E/Z)-3-(3-(5-(4-fluorophenyl)-2-penten-4-yn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2,2,1]heptane,

Endo 3-(3-(2-pyridyl)-2-propyn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

25 Endo 3-(3-(3-furyl)-2-propyn-1-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-(2,2,3,3,4,4,4-heptafluorobutyl-1-oxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-(3-(3-fluorophenyl)-2-propyn-1-yloxy)-1.2.5-thiadiazol-4-yloxy-1-azabicyclo[2.2.1]heptane,

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Endo 3-(3-(3,3,3-trifluoropropylthio)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,

- 5 Endo 3-(3-(4,4,4-trifluorobutylthio)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,
 - Endo 3-(3-[4-cyanobenzylthio]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,
 - Endo 3-(3-[2-cyanoethylthio]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,
 - Endo 3-(3-[2,4-difluorobenzylthio]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,
 - Endo 3-(3-[2-fluoroethyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo-[2.2.1]heptane,
- 20 Endo 3-(3-butylsulfonyl-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,
 - Endo 3-(3-[3-(3-thienyl)-2-propyn-1-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,
- Endo 3-(3-[3-(2-thienyl)-2-propyn-1-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,
 - Endo 3-(3-[1-cyclopropylethyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabi-cyclo[2.2.1]heptane,
 - Endo 3-(3-[1-(3-fluorophenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

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Endo 3-(3-[1-(4-fluorophenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

- 5 Endo 3-(3-[1-(2-thienyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,
 - Endo 3-(3-[1-(3-chlorophenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-(3-chlorophenyl)-2-propynyl-1-oxy)-1,2,5-thiadiazol-4-yloxy]-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-(3,5-difluorophenyl)-2-propynyl-1-oxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[1-(2-pyridyl)-4-methyl-1-pentyn-3-yloxy)-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

- 20 Endo 3-(3-[1-(3,5-dichlorophenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,
 - Endo 3-(3-[1-(3,5-difluorophenyl)-4-methyl-1-pentyn-3-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

Endo 3-(3-[3-(2-thiazolyl)-2-propyn-1-yloxy]-1,2,5-thiadiazol-4-yloxy)-1-azabicyclo[2.2.1]heptane,

or a pharmaceutically acceptable salt or solvate thereof.

13. A method of preparing a compound according to claim 1, characterized in

a) reacting a compound of formula !!

(II)

with first HSR⁴/Et₂NH and subsequently S₂Hal₂, wherein R⁴ has the meaning defined above, to form a compound of formula III

(111)

wherein R⁴ has the meaning defined above; or the compound of formula II is first reacted with HOR⁴/Et₃N and subsequently with S₂Hal₂, wherein R⁴ has the meaning defined above, to form a compound of formula IV

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wherein R⁴ has the meaning defined above; and a compound of formula III or formula IV can subsequently be reacted in the presence of an alkoxide metal with a compound of formula V

(V)

(VII)

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wherein G, r and W have the meanings defined above, to form a compound of formula VI selected from the following

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$$G-(CH_2)_r-W$$

$$N$$

$$(VI)$$

$$(O,S)R^4$$

wherein G, R, W and R⁴ have the meanings defined above; or

b) a compound of formula III can be oxidized to form a compound of formula VII

wherein R⁴ has the meaning defined above, which subsequently can be reacted with a compound of formula V to form a compound of formula VIII

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wherein G, r and W have the meanings defined above which compound can subsequently be reacted with either R-OH or RMgHal to form a compound of formula I; or

c) a compound of formula VI

wherein G, r, W and R^4 have the meanings defined above, can be oxidized to form a compound of formula IX

$$G(CH_2)_r$$
 N
 SO_2R^4
(IX)

- wherein G, r, W and R⁴ have the meanings defined above which compound subsequently can be reacted with either R-OH or RMgHal to form a compound of formula I.
 - 14. A pharmaceutical composition comprising a compound according to claim1 together with one or more pharmaceutically acceptable carriers or diluents.

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- 15. A pharmaceutical composition for use in treating a disease in the central nervous system caused by malfunctioning of the muscarinic cholinergic system comprising an effective amount of a compound according to claim 1 together with a pharmaceutically acceptable carrier or diluent.
- 16. The pharmaceutical composition according to claim 14 of 15 in the form of an oral dosage unit or parenteral dosage unit.
- 17. The pharmaceutical composition according to claim 16, wherein said dosage unit comprises from about 0.1 to about 100 mg of the compound according to claim 1.
- 18. A method of treating a disease in the central nervous system caused by malfunctioning of the muscarinic cholinergic system comprising administering to a subject in need thereof a pharmaceutically effective amount of a compound according to claim 1.
- 19. A method of treating a disease in the central nervous system caused by malfunctioning of the muscarinic cholinergic system comprising administering to a subject in need thereof a pharmaceutical composition according to claims 14 to 17.
- 20. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof for the preparation of a medicament for treatment of a disease in the central nervous system caused by malfunctioning of the muscarinic cholinergic system.
- 21. A method for treating a condition associated with the modulation of a muscarinic cholinergic receptor comprising administering to a subject in need thereof a pharmaceutically effective amount of a compound according to claim 1.

- 22. The use of a compound according to claim 1 or a pharmaceutically acceptable salt thereof for the preparation of a medicament for treatment of a condition associated with the modulation of a muscarinic cholinergic receptor.
- 5 23. A method for interacting with a muscarinic cholinergic receptor comprising administering to a subject in need thereof an effective amount of a compound according to claim 1.
 - 24. The use of a compound according to claim for a pharmaceutically acceptable salt hereof for the preparation of a medicament for interacting with a muscarinic cholinergic receptor.